# General

## Guideline Title

The clinical utility of sperm DNA integrity testing: a guideline.

## Bibliographic Source(s)

Practice Committee of the American Society for Reproductive Medicine. The clinical utility of sperm DNA integrity testing: a guideline. Fertil Steril. 2013 Mar 1;99(3):673-7. [45 references] PubMed

## Guideline Status

This is the current release of the guideline.

# Recommendations

## Major Recommendations

Definitions for the strength of the recommendations (Level A-C) are given at the end of the "Major Recommendations" field.

Summary

- Existing data do not support a consistent relationship between abnormal deoxyribonucleic acid (DNA) integrity and reproductive outcomes
- At present, the results of sperm DNA integrity testing alone do not predict pregnancy rates achieved through natural conception or with intrauterine insemination (IUI), in vitro fertilization (IVF), or intracytoplasmic sperm injection (ICSI). However, further re-search may lead to validation of the clinical utility of these tests.

Recommendation

There is insufficient evidence to recommend the routine use of sperm DNA integrity tests in the evaluation and treatment of the infertile couple (Level C).

Definitions:

Level A: There is good evidence to support the recommendations, either for or against.

Level B: There is fair evidence to support the recommendations, either for or against.

Level C: There is insufficient evidence to support a recommendation, either for or against.

## Clinical Algorithm(s)

None available

# Scope

## Disease/Condition(s)

Male infertility

## Guideline Category

Diagnosis

Technology Assessment

## Clinical Specialty

Medical Genetics

Urology

## Intended Users

Physicians

## Guideline Objective(s)

To assess the evidence pertaining to the clinical utility of sperm deoxyribonucleic acid (DNA) integrity testing and target areas that require more study

## Target Population

Infertile men

## Interventions and Practices Considered

The following sperm deoxyribonucleic acid (DNA) integrity tests were considered but there is insufficient evidence to recommend their routine use:

- Sperm chromatin structure assay (SCSA)
- Deoxynucleotidyl transferase-mediated deoxynucleotide triphosphate (dUTP) nick end labeling assay (TUNEL)
- Single-cell gel electrophoresis assay (COMET)
- Sperm chromatin dispersion test (SCD)

## Major Outcomes Considered

- Likelihood ratios
- Pregnancy and fertilization rates
- Association of sperm deoxyribonucleic acid (DNA) damage with reproductive outcomes

# Methodology

## Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

A systematic literature search was performed using the search strategy: sperm AND (DNA OR chromatin) AND (fragmentation OR damage OR integrity) AND (pregnancy [title/abstract] OR embryo [title/abstract]) AND (Humans [mesh] AND English [language]) (204 citations). The search was restricted to MEDLINE citations published in the English language from 1966 to November 2011. Studies were eligible if they met one of the following criteria: primary evidence (clinical trials) that assessed the predictive potential using predictive statistics, meta-analyses, and relevant articles from bibliographies of identified articles.

## Number of Source Documents

The comprehensive literature search yielded 74 citations eligible for full review.

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Level I: Evidence obtained from at least one properly designed randomized controlled trial.

Level II-1: Evidence obtained from well-designed controlled trials without randomization.

Level II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

Level II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.

Level III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

## Description of the Methods Used to Analyze the Evidence

Assessment of the Sperm Deoxyribonucleic Acid (DNA) Integrity Testing Literature

Review articles found during the comprehensive literature search were excluded, while meta analyses were included in the review. Twenty studies used the deoxynucleotidyl transferase-mediated deoxynucleotide triphosphate (dUTP) nick end labeling (TUNEL) assay to assess deoxyribonucleic acid (DNA) integrity while 28 employed the sperm chromatin structure assay (SCSA) test. The single-cell gel electrophoresis assay (COMET) test was used in 9 papers while the sperm chromatin dispersion test (SCD) test was used in 5. Less commonly used assays were assessed in 5 or fewer publications.

Overall, there are no Level I studies as would be expected for a predictive diagnostic clinical test. In addition, there are few high-quality

prospective studies recruiting consecutive patients validating previously established cut-points with gold standard fertility outcomes. Most studies present Level II-2 evidence or less. The majority of studies are hindered by small sample size, non-consecutive recruitment of patients, variable patient populations, lack of control for female factors (particularly age), weak statistical methodology in calculating threshold values and predictive ability of tests, and use of several different methods for assessing DNA damage.

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

For a diagnostic test to be clinically useful the results must be reproducible, applicable to a given patient, and change the management of the patient. For tests of deoxyribonucleic acid (DNA) integrity to be clinically important there must be an association of sperm DNA damage with reproductive outcomes. The literature was reviewed to answer the following questions:

- Does the DNA integrity test predict male fertility with natural conception?
- Does the DNA integrity test predict pregnancy with intrauterine insemination (IUI)?
- Is DNA fragmentation predictive of pregnancy with in vitro fertilization (IVF)?
- Is DNA fragmentation predictive of pregnancy with IVF and intracytoplasmic sperm injection (ICSI)?
- Is DNA fragmentation predictive of pregnancy loss?

## Rating Scheme for the Strength of the Recommendations

Level A: There is good evidence to support the recommendations, either for or against.

Level B: There is fair evidence to support the recommendations, either for or against.

Level C: There is insufficient evidence to support a recommendation, either for or against

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Internal Peer Review

## Description of Method of Guideline Validation

The Practice Committee and the Board of Directors of the American Society for Reproductive Medicine (ASRM) have approved this report.

This document was reviewed by ASRM members and their input was considered in the preparation of the final document.

# Evidence Supporting the Recommendations

## Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

# Benefits/Harms of Implementing the Guideline Recommendations

## Potential Benefits

Proper use of sperm deoxyribonucleic acid (DNA) integrity testing

## Potential Harms

Not stated

# Qualifying Statements

## Qualifying Statements

- Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations.
- Sperm deoxyribonucleic acid (DNA) damage is more common in infertile men and may contribute to poor reproductive performance. However, current methods for assessing sperm DNA integrity do not reliably predict treatment outcomes and cannot be recommended routinely for clinical use.

# Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Living with Illness

## IOM Domain

Effectiveness

Patient-centeredness

# Identifying Information and Availability

## Bibliographic Source(s)

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## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2013 Mar 1

## Guideline Developer(s)

American Society for Reproductive Medicine - Nonprofit Organization

## Source(s) of Funding

American Society for Reproductive Medicine

## Guideline Committee

The Practice Committee of the American Society for Reproductive Medicine

## Composition of Group That Authored the Guideline

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## Financial Disclosures/Conflicts of Interest

All Committee members disclosed commercial and financial relationships with manufacturers or distributors of goods or services used to treat patients. Members of the Committee who were found to have conflicts of interest based on the relationships disclosed did not participate in the discussion or development of this document.

## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available from the American Society for Reproductive Medicine Web site .

Print copies: Available from American Society for Reproductive Medicine, 1209 Montgomery Highway, Birmingham, Alabama 35216-2809; Phone: (205) 978-5000; Fax: (205) 978-5005; E-mail: asrm@asrm.org; Web site: www.asrm.org.

## Availability of Companion Documents

The following is available:

- CME credit related to this guideline is available from the American Society for Reproductive Medicine Web site.

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on June 27, 2014. The information was verified by the guideline developer on July 22, 2014.

## Copyright Statement



# Disclaimer

## NGC Disclaimer